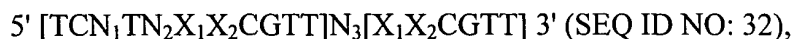


wherein X_1X_2 is selected from the group consisting of GT, GA, and AT, wherein at least one nucleotide has a phosphate backbone modification, and wherein C of CpG is unmethylated. In some embodiments, X_1 is G. In some embodiments, the adjuvant-type CpG nucleic acid has a sequence including at least the following formula:



wherein N₃ is about 0-26 nucleotides, N₃ may not in some embodiments contain a CCGG quadmer or more than one CCG or CGG trimer. N₃ may optionally be selected from the group consisting of nothing, any nucleotide, C, T, TT, TTT, TTTT, and TC. In some embodiments, N₃ is a single pyrimidine. In other embodiments, N₃ is at least two pyrimidines. In certain embodiments, N₃ is 0 nucleotides. In other embodiments N₃ is 1 nucleotide. In yet other embodiments, N₃ is at least 2 nucleotides.

In some embodiments, the adjuvant-type CpG nucleic acid has a sequence including at least the following formula:



wherein N₄ is about 0-26 bases and with the proviso that N₄ may not contain a CCGG quadmer or more than one CCG or CGG trimer. In some embodiments, N₄ is selected from the group consisting of nothing, any nucleotide, C, T, TT, TTT, TTTT, and TC. In certain embodiments, N₃ and N₄ are both TT. In some embodiments, X₂ is T. In some embodiments, X₁ is G. In certain embodiments, the adjuvant-type CpG nucleic acid has a sequence including at least one of the following formulas:



Optionally, the immunostimulatory nucleic acid has a sequence including at least the following formula:



Page 14, line 14 through page 15, line 1.

Optionally, the immunostimulatory nucleic acid has a sequence including at least the following formula:



TCGTCGTTTTGTCGTTTTGTCGTTTTT (SEQ ID NO: 35),

TCGTCGTTTTGTCGTTTTGTCGTTCCC (SEQ ID NO: 36),

TCGTCGTTTTGTCGTTTTGTCGTTAAA (SEQ ID NO: 37), or

TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID NO: 38).

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Table 1. Exemplary CpG nucleic acids

ATCGACTCTCGAGCGTTCTC	(SEQ ID NO:39)
ATCGACTCTCGAGCGTTZTC	(SEQ ID NO:40)
TCCACGACGTTTTTCGACGTT	(SEQ ID NO:41)
TCCATAACG TTCCTGATGCT	(SEQ ID NO:42)
TCCATAGCG TTCCTAGCGTT	(SEQ ID NO:43)
TCCATCACGTGCCTGATGCT	(SEQ ID NO:44)
TCCATGACGGTCCTGATGCT	(SEQ ID NO:45)
TCCATGACGTCCCTGATGCT	(SEQ ID NO:46)
TCCATGACG TTCCTGACGTT	(SEQ ID NO:47)
TCCATGACG TTCCTGATGCT	(SEQ ID NO:48)
TCCATGCCGGTCCTGATGCT	(SEQ ID NO:49)
TCCATGCGTTGCGTTGCGTT	(SEQ ID NO:50)
TCCATGGCGGTCCTGATGCT	(SEQ ID NO:51)
TCCATGTCGATCCTGATGCT	(SEQ ID NO:52)
TCCATGTCGCTCCTGATGCT	(SEQ ID NO:53)
TCCATGTCGGTCCTGATGCT	(SEQ ID NO:54)
TCCATGTCGGTCCTGCTGAT	(SEQ ID NO:55)
TCCATGTCGGTZCTGATGCT	(SEQ ID NO:56)
TCCATGTCG TTCCTGATGCT	(SEQ ID NO:57)
TCCATGTCG TTCCTGTCGTT	(SEQ ID NO:58)
TCCTGACG TTCCTGACGTT	(SEQ ID NO:59)

TCCTGTCGTTTCCTGTCGTT	(SEQ ID NO:60)
TCCTGTCGTTTCCTTGTCGTT	(SEQ ID NO:61)
TCCTGTCGTTTTTTTGTCGTT	(SEQ ID NO:62)
TCCTTGTCGTTTCCTGTCGTT	(SEQ ID NO:63)
TCGTCGCTGTTGTCGTTTCTT	(SEQ ID NO:64)
TCGTCGTCGTCGTT	(SEQ ID NO:65)
TCGTCGTTGTCGTTGTCGTT	(SEQ ID NO:66)
TCGTCGTTGTCGTTTTGTCGTT	(SEQ ID NO:67)
TCGTCGTTTTGTCGTTTTGTCGTT	(SEQ ID NO:29)
TCTCCCAGCGCGCGCCAT	(SEQ ID NO:68)
TGTCGTTGTCGTT	(SEQ ID NO:69)
TGTCGTTGTCGTTGTCGTT	(SEQ ID NO:70)
TGTCGTTGTCGTTGTCGTTGTCGTT	(SEQ ID NO:71)
TGTCGTTTGTCGTTTGTCGTT	(SEQ ID NO:72)

In a preferred embodiment of the invention, the IFN- α -inducing CpG nucleic acid comprises a base sequence

5' Y₁N₁X₁X₂CGX₃X₄N₂Y₂ 3' (SEQ ID NO: 73),

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wherein G is guanine; C is unmethylated cytosine; X₁, X₂, X₃, and X₄ independently are single nucleotides; N₁ and N₂ are independently nucleic acid molecules each having between 0 and 20 nucleotides; N₁X₁X₂CGX₃X₄N₂ (SEQ ID NO: 74) includes a palindrome at least 6 nucleotides long that contains at least one CG; Y₁ is a nucleic acid molecule having between 1 and 8 nucleotides comprising at least one modified internucleotide linkage; and Y₂ is independently a nucleic acid molecule having between 3 and 8 nucleotides comprising at least 3 consecutive Gs and at least one modified internucleotide linkage. In some embodiments, at least one modified internucleotide linkage is a phosphorothioate modified linkage. In certain embodiments, Y₁ is comprised of at least 3 Gs. In certain embodiments, Y₁ is comprised of at least 4 Gs. In other embodiments, Y₁ is comprised of at least 7 Gs. In some embodiments Y₁ is comprised of all Gs. In some embodiments Y₂ is comprised of at least 4 Gs. In other embodiments, Y₂ is comprised

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of at least 7 Gs. In yet other embodiments, Y_2 is comprised of all Gs. In some embodiments, Y_1 includes at least two modified internucleotide linkages and Y_2 includes at least two modified internucleotide linkages. In certain embodiments, Y_1 includes between two and five modified internucleotide linkages and Y_2 includes between two and five modified internucleotide linkages. In some embodiments, the palindrome has a phosphodiester backbone. In other embodiments, the IFN- α -inducing CpG nucleic acid as a whole has a backbone made up entirely of modified internucleotide linkages. In certain embodiments, the IFN- α -inducing CpG nucleic acid is ODN 2306 (ggGGACGTCGACGTggggG) (SEQ ID NO: 30).

In the Claims:

Please cancel claims 40-53 and 55-86.

Please amend the claims as follows:

25. (Amended) The method of claim 3, wherein the adjuvant-type CpG nucleic acid has a sequence including at least the following formula:

5'[TCN₁TN₂X₁X₂CGTT]N₃[X₁X₂CGTT]N₄[X₁X₂CGTT] 3' (SEQ ID NO: 33),

wherein N₄ is about 0-26 bases with the proviso that N₄ does not contain a CCGG quadmer or more than one CCG or CGG trimer.

30. (Amended) The method of claim 4, wherein the IFN- α -inducing CpG nucleic acid comprises the following sequence

5' Y₁N₁X₁X₂CGX₃X₄N₂Y₂ 3' (SEQ ID NO: 73),

wherein G is guanine; C is unmethylated cytosine; X₁, X₂, X₃, and X₄ independently are single nucleotides; N₁ and N₂ are independently nucleic acid molecules each having between 0 and 20 nucleotides; N₁X₁X₂CGX₃X₄N₂ (SEQ ID NO: 74) includes a palindrome at least 6 nucleotides long that contains at least one CG; Y₁ is a nucleic acid molecule having between 1 and 8 nucleotides comprising at least one modified internucleotide linkage; and Y₂ is independently a nucleic acid molecule having between 3 and 8 nucleotides comprising at least 3 consecutive Gs and at least one modified internucleotide linkage.